REMARKS

The Office Action mailed August 12, 2004 has been received and reviewed. Claims 7 through 11 and 19 through 29 are identified as pending in the Office Action. Applicants have amended claims 7, 10, 11, 19, 20, 21, 22, and 29, canceled claims 8 and 9, and added new claims 30 through 35. Claims 1 to 6 and 12 to 18 were previously canceled. All amendments and cancellations have been made without prejudice or disclaimer. Reconsideration of the application as amended is respectfully requested.

Support for the claim amendments may be found at page 5, lines 5 through 25, page 9 line 23 through page 10, line 18 and a page 12 line 1 through page 13, line 4 of the as-filed specification.

Applicants note the objection to specification, the objection to claim 20, and the rejection of claim 21 under 35 U.S.C. § 112, Second Paragraph, are all withdrawn in the Office Action.

Interview

Applicants thank the Examiner for the courtesy extended during the interview conducted on December 8, 2004. Applicant appreciates the Examiner's helpful comments. At the interview, the coverage of the claims was discussed with particular attention to enablement of claims directed to "marking vaccines." This amendment is based on the discussion at the interview and the Examiner's assistance provided therein.

35 U.S.C. § 112, First Paragraph, Rejections

The rejection of claims 7 through 11, 19 and 20 and new claims 22 through 29 under 35 U.S.C. § 112, first paragraph as assertedly lacking enablement was maintained from the previous Office Action. Applicants respectfully submit that independent claims 7, 19, 22, and 29 are enabled, as are the claims dependent therefrom.

The Office Action notes that applicants earlier amended the claims to "marker vaccines," but concludes the arguments in support of enablement "are not persuasive" as the "Examiner disagrees with Applicant's assertion that that 'claims 7 and 19 are directed to a marker vaccine that allows exposure of an animal to a wild-type strain to be detected" (Office Action at page 8). The Office Action states that these claims are instead "directed to a vaccine comprising an

immunologically effective amount of a mutated bacterium being selected from the group consisting of the *Salmonella* species *tymphiurium, enterditidis, choleraesuis, dublin, abortus-ovi, abortus-equi, derby, hadar, heidelberg, agona* and *arizonae* that in its wild-type form carries flagella said mutated bacterium lacking flagellin." *Ibid*, underlining in original). The Office Action states that "the term 'vaccine' encompasses the ability of the specific antigen to induce protective immunity to *Salmonella* infection or disease induction." (Office Action at page 3).

Applicants respectfully submit that amended independent claims 7 and 19 are no longer directed to "vaccines." Instead, these amended claims are directed to "immunogenic compositions for marking exposure of a subject to wild-type *Salmonella*." Similarly, claims 22 and 29 are now directed to the "improvement" of vaccines, with claim 22 directed to an improved vaccine and claim 29 directed to an improved marker vaccine. As discussed in the previous response, the present specification provides support for the present claims.

Specifically, Example 3 of the specification demonstrates that inoculations using two different vaccine strains, comprising STMP and STM2000, were able to reduce fecal shedding of a challenge strain significantly and that STMP and STM2000 inoculated chickens survived compared to an 80% death rate for those inoculated with a wildtype vaccine. Further, Example 4, at pages 22-23 of the specification, shows that administration with live attenuated flagella-less *S. typhimurium* according to the present invention gives excellent results in pigs. Even more support is provided by Example 2, at page 18 of the specification, which discloses vaccines comprising flagellated and non-flagellated *Salmonellas,* specifically *S. entireditis* fla^+ and *S. entireditis* fla^-. The results of Example 2 show that *S. entireditis* fla^- vaccines also provide a clearly recognizable marker. The present specification thus teaches effective marking using *Salmonella* bacteria lacking flagellin, other than STM2000, and provides support for additional strains at page 6, lines 4-15 and page 9, lines 10-12. Accordingly, it is respectfully submitted that the amended independent claims 7, 19, 22, and 29, with the claims dependent therefrom are fully enabled.

Further, with respect to independent claims 20 and 22, applicants note that the Office Action again repeats the earlier examination of the Whadan, Lockman and Hackett references, to support a rejection based on an asserted lack of establishing protectiveness of all strains. The Office Action concludes that:

> It should be noted that claims are not so limited to *Salmonella* bacterium that have mutation/mutations is in only genes associated with synthesis of the flagella. The claims merely recite "mutated bacterium ... that in its wild-type form carries flagella, said mutated bacterium lacking flagellin". Thus, the claims do not define the actual mutation/mutations that are made in the *Salmonella* bacterium. One of skill in the art would not conclude that all strains of *Salmonella* encompassed by the claimed invention are protective based on the teachings of the prior art. Therefore, the specification is only enabled for vaccine compositions for the protection against Salmonellosis comprising an immunologically effective amount of a *Salmonella typhimurium* STMP mutated bacterium and a pharmaceutical carrier. (Office Action at page 9, underlining in original).

Amended claim 20 now recites "an immunologically effective amount of a mutated *Salmonella typhimurium* bacterium that in its wild type form carries flagella, **said mutated *Salmonella typhimurium* bacterium not capable of inducing an immune response to flagellin due to a mutation in a gene of the flagellar biogenesis pathway**." Similarly, amended claim 22 now recites "a *Salmonella* bacterium which is a mutated bacterium that in its wild type form carries flagella, but **is no longer capable to induce an immune response to flagellin due to a mutation in a gene of the flagellar biogenesis pathway**." Accordingly, these claims now "define the actual mutation/mutations that are made in the *Salmonella* bacterium." Further, as noted previously herein, Examples 3 and 4 of the specification disclose protective effects of multiple strains of *Salmonella typhimurium* strains. Additionally, Example 2 discloses a *S. entireditis* vaccine. Applicants respectfully submit claims 20 and 22, with the claims dependent therefrom, are thus enabled and request they be allowed.

With respect to claims 22 and 29, as explained in the as-filed specification in the paragraph beginning at page 4, line 9, the present invention includes the surprising result that an improvement over existing *Salmonella* vaccines may be obtained by making marker vaccines from known *Salmonella* vaccine strains using the flagellar biogenesis pathway. Support for the amendment of claim 29 may be found at page 9, lines 14 to 21 of the as-filed specification. As shown by the examples, discussed previously herein, such improved vaccines and improved marker vaccines are enabled by the instant specification.

35 U.S.C. § 102 Rejections

Claims 7, 8, 20, 22 through 25 and 29 were rejected in the Office Action as assertedly being anticipated under 35 U.S.C. § 102(b) by Joys et al. (*Journal of General Microbiology*, vol. 41, pp. 47-55, 1965) ("Joys"). Claim 8 is canceled herein, rendering this rejection moot as to it. Applicants respectfully submit that amended independent claims 7, 19, 20, 21, 22 and 29 define over the cited reference.

The Office Action states that Joys teaches "compositions comprising fla- *Salmonella typhimurium* bacterium in broth culture" and that other claim limitations "are being viewed as limitations of intended use." (Office Action at pages 10 to 11).

As amended, independent claim 7 contains the elements of "an adjuvant." Since Joys merely discloses the presence of *Salmonella* bacteria in broth and does not disclose any compositions including an adjuvant, claim 7, with the claims dependent therefrom defines thereover.

With respect to amended independent claim 20, it now contains the elements of pharmaceutically acceptable carrier comprising water, a solution of physiological salt concentration, SPGA, sorbitol, mannitol, starch, sucrose, glucose, dextran, albumin, casein, bovine serum, skim milk, or phosphate buffer." Joys merely discloses the presence of *Salmonella* bacteria in broth, and, does not teach these pharmaceutically acceptable carriers. Accordingly, it is respectfully submitted that claim 20, with the claims dependent therefrom defines over the Joys reference.

With respect to amended independent claims 19, 22, and 29, each of these claims includes the elements of the "mutated bacterium being inactivated" and "an adjuvant." As these elements are not disclosed in Joys, claims 19, 22 and 29, together with the claims dependent therefrom are not anticipated thereby.

35 U.S.C. § 103 Rejections

Claims 7, 8, 11, 20, 22 through 25, 28 and 29 were rejected in the Office Action as assertedly being obvious anticipated under 35 U.S.C. § 103(a) over Joys in view of U.S. Patent

5,665,363 to Hansen et al. ("Hansen"). Applicants respectfully submit that amended independent claims 7, 19, 20, 21, 22 and 29 define over the cited references.

As noted previously herein, the Office Action states that Joys teaches "compositions comprising fla- *Salmonella typhimurium* bacterium in broth culture" and that other claim limitations "are being viewed as limitations of intended use." It then states that Hansen teaches "that pharmaceutical compositions comprising live or killed microorganisms can be freeze-dried or spray-dried." (Office Action at page 12). From these two statements the Office Action then concludes that it would have been obvious "to freeze-dry the compositions comprising fla- *Salmonella typhimurium* bacterium as taught by Joys et al because Hansen et al teach that pharmaceutical compositions comprising live or killed microorganisms can be freeze-dried or spray-dried." (Office Action at pages 12-13).

Joys is directed to a complementation study performed by transduction of *Salmonella* bacterial cultures. This reference does not disclose, teach, or suggest the use of such cultures as a pharmaceutical compound. Applicants note that the Federal Circuit has repeatedly cautioned against employing hindsight by using the applicant's disclosure as a blueprint to reconstruct the claimed invention out of isolated teachings of the prior art. *See, e.g., Grain Processing Corp. v. American-Maize Prods. Co.*, 5 U.S.P.Q.2d 1788, 1792 (Fed. Cir. 1988).

"That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown." *Application of Spormann*, 150 USPQ 449, 452 (CCPA 1966). The Office Action bases this rejection on a conclusion that the *Salmonella* bacterial cultures of Joys are inherently vaccines. Since the rejection is based on what the Office asserts to be an inherent, but unknown property of Joys, that reference cannot be combined with Hansen to produce an obviousness rejection. *Id*

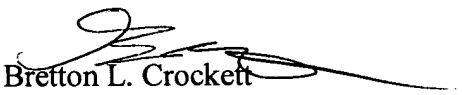
Further, M.P.E.P. 2143.01 explains that if "the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious." (citing *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959)). Further, "[i]f a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification." (citing, *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)). Applicants respectfully submit

that freeze-drying the *Salmonella* bacterial cultures, as suggested by the Office Action, would change the principle of operation of the Joy cultures, which are used for transduction studies performed by diluting broth cultures, thereby rendering the cultures unsatisfactory for their intended purpose of transduction studies. Accordingly, a requisite motivation to combine is lacking and the rejection should be withdrawn.

CONCLUSION

All pending claims are believed to be in condition for allowance, and an early notice thereof is respectfully solicited. Should the Office determine that additional issues remain which might be resolved by a telephone conference, the Examiner is respectfully invited to contact applicants' attorney.

Respectfully submitted,



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